BONE

Liposomes containing phosphatidylserine inhibit osteoclastogenesis in rats

Phosphatidylserine-containing liposomes (PSLs), which can mimic the effects of apoptotic cells, actively suppress the inflammatory response by phagocytes and inhibit the maturation of dendritic cells. The effects of PSLs on osteoclastogenesis are, however, less well understood. A new study from researchers in Japan suggests that PSLs inhibit osteoclast differentiation and trabecular bone loss through the secretion of the anti-inflammatory molecules transforming growth factor-β1 (TGF-β1) and prostaglandin E2 (PGE2).

> “...PSLs could represent a potential pharmacologic treatment to prevent abnormal bone loss...”

The investigators examined these effects of PSLs on osteoclastogenesis both *in vitro*, using cultures of rat bone marrow cells and of osteoclast precursor cells, and also *in vivo*, in rats with adjuvant-induced arthritis, a widely used model of osteoclast-induced trabecular bone loss.

In vitro, PSLs were phagocytosed by osteoclast precursor cells and inhibited osteoclastogenesis but without affecting the formation of osteoclast precursors. PSLs induce the secretion of TGF-β1 and PGE2 by the cultured cells after phagocytosis by osteoclast precursor cells. Expression levels of receptor activator of nuclear factor κB (RANK), RANK ligand (RANKL), ICAM-1 and CD44—molecules with essential roles in the differentiation of osteoclast prescursor cells—were downregulated in cultured cells treated with PSLs.

Consistent with the results from cell cultures, *in vivo* treatment with PSLs led to decreased expression of RANK, RANKL and ICAM-1 messenger RNA in the skeletal tissues of rats with adjuvant-induced arthritis. By contrast, levels of secretion of TGF-β1 and PGE2 in the plasma of these rats were substantially increased. Quantification of the trabecular bone network of ankle joint bones showed that the osteoclast-induced loss of trabecular bone was markedly improved by treatment with either PSLs or the combination of TGF-β1 and PGE2.

Together, the results show that PSLs phagocytosed by myeloid osteoclast precursors inhibit osteoclastogenesis and osteoclast-induced trabecular bone loss in rats, potentially through TGF-β1 and PGE2. Since phosphatidylserine is a component of the cell membrane, the authors suggest that PSLs could represent a potential pharmacological treatment to prevent abnormal bone loss, but the clinical potential of this approach remains to be investigated.

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